

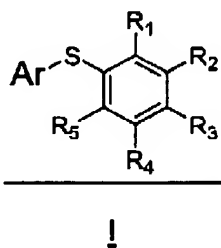
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Attorney Docket No. 09095.0006-01

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions and listings of claims in the application:

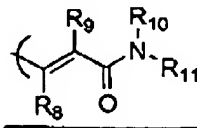
Claims 1-26 (cancelled).

27. (currently amended) A compound according to ~~Claim 4~~ of formula I



or a pharmaceutically-acceptable salt or prodrug thereof.

wherein R<sup>1</sup> is haloalkyl; R<sup>2</sup> is haloalkyl; R<sup>3</sup> is trans-cinnamide wherein trans-cinnamide is defined as



"trans-cinnamide"

wherein R<sup>8</sup> and R<sup>9</sup> are hydrogen and R<sup>10</sup> and R<sup>11</sup> together with N are heterocyclyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is hydrogen; and Ar is aryl, wherein the aryl is substituted with a substituted heterocyclyl,

wherein the heterocyclyl is chosen from 4-, 5-, 6- and 7-membered rings containing 1-3 heteroatoms independently selected from nitrogen, oxygen and sulfur; the 4- and 5-membered rings have zero to two double bonds and the 6-

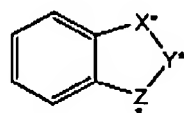
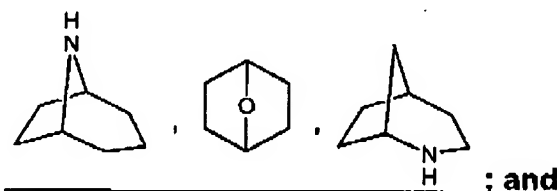
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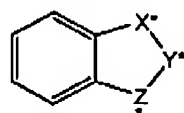
and 7-membered rings have zero to three double bonds, the heterocyclyl being optionally substituted with alkyl, halogen, hydroxy or alkoxy substituents,

wherein the heterocyclyl optionally comprises a group chosen from:

(i) bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring, and another monocyclic heterocyclic ring;

(ii) bridged bicyclic groups where a monocyclic heterocyclic group is optionally bridged by an alkylene group selected from



(iii) compounds of the formula  where X\* and Z\* are independently selected from -CH<sub>2</sub>-, -CH<sub>2</sub>NH-, -CH<sub>2</sub>O-, -NH- and -O-, with the proviso that at least one of X\* and Z\* is not -CH<sub>2</sub>-, and Y\* is selected from -C(O)- and -(C(R''))<sub>v</sub>-, where R'' is hydrogen or alkyl of one to four carbons, and v is 1-3;

and wherein aryl is defined as a mono- or bicyclic carbocyclic, aromatic ring.

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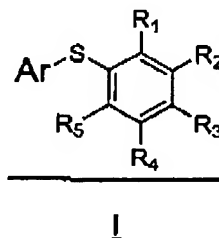
28. (currently amended) A compound according to Claim ~~[[1]]~~ 27 wherein  $R^1$  is trifluoromethyl;  $R^2$  is trifluoromethyl;  $R^3$  is trans-cinnamide wherein  $R^8$  and  $R^9$  are hydrogen and  $R^{10}$  and  $R^{11}$  together with N are morpholino;  $R^4$  is hydrogen;  $R^5$  is hydrogen; and Ar is phenyl, wherein the phenyl is substituted with substituted piperidine.

29. (currently amended) A compound according to Claim ~~[[12]]~~ 28 that is [3-(3-carboxypiperidin-1-yl)phenyl] [2,3-bis(trifluoromethyl)-4-(E-((4-morpholino)carbonyl)ethenyl)phenyl]sulfide.

30. (currently amended) A compound according to Claim ~~[[12]]~~ 28 that is (R)-[3-(3-carboxypiperidin-1-yl)phenyl] [2,3-bis(trifluoromethyl)-4-(E-((4-morpholino)carbonyl)ethenyl)phenyl]sulfide.

31. (currently amended) A compound according to Claim ~~[[12]]~~ 28 that is (S)-[3-(3-carboxypiperidin-1-yl)phenyl] [2,3-bis(trifluoromethyl)-4-(E-((4-morpholino)carbonyl)ethenyl)phenyl]sulfide.

32. (currently amended) A method of treating cerebral vasospasm comprising the administration ~~of a compound of Claim 1~~ to a mammal in need of treatment, of a therapeutically effective amount of a compound of formula I



or a pharmaceutically-acceptable salt or prodrug thereof.

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wherein  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ , and  $R_5$  are independently selected from

- a. hydrogen,
- b. halogen,
- c. alkyl,
- d. haloalkyl,
- e. alkoxy,
- f. cyano,
- g. nitro,
- h. carboxaldehyde, and

with the proviso that at least one of  $R_1$  or  $R_3$  is a "cis-cinnamide" or a

"trans-cinnamide", defined as



wherein  $R_8$  and  $R_9$  are independently selected from

- a. hydrogen,
- b. alkyl,
- c. carboxy alkyl,
- d. alkylaminocarbonyl alkyl, and
- e. dialkylaminocarbonyl alkyl,

wherein  $R_{10}$  and  $R_{11}$  are independently selected from

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- a. hydrogen,
- b. alkyl,
- c. cycloalkyl,
- d. alkoxycarbonylalkyl,
- e. hydroxyalkyl,
- f. substituted aryl,
- g. heterocyclyl,
- h. heterocyclylalkyl,
- i. heterocyclylamino,
- j. substituted heterocyclyl, and
- k. substituted heterocyclylalkyl,

or wherein NR<sub>10</sub>R<sub>11</sub> is heterocyclyl or substituted heterocyclyl, where  
substituents are independently selected from

- 1) alkyl,
- 2) alkoxy,
- 3) alkoxyalkyl,
- 4) cycloalkyl,
- 5) aryl,
- 6) heterocyclyl,
- 7) heterocyclylcarbonyl,
- 8) heterocyclylalkylaminocarbonyl,
- 9) hydroxy,
- 10) hydroxyalkyl,

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- 11) hydroxyalkoxyalkyl,
- 12) carboxy,
- 13) carboxyalkyl,
- 14) carboxycarbonyl,
- 15) carboxaldehyde,
- 16) alkoxycarbonyl,
- 17) arylalkoxycarbonyl,
- 18) aminoalkyl,
- 19) aminoalkanoyl,
- 20) carboxamido,
- 21) alkoxycarbonylalkyl,
- 22) carboxamidoalkyl,
- 23) cyano,
- 24) tetrazolyl,
- 25) substituted tetrazolyl,
- 26) alkanoyl,
- 27) hydroxyalkanoyl,
- 28) alkanoyloxy,
- 29) alkanoylamino,
- 30) alkanoyloxyalkyl,
- 31) alkanoylaminoalkyl,
- 32) sulfonate,
- 33) alkylsulfonyl,

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34) alkylsulfonylaminocarbonyl,

35) arylsulfonylaminocarbonyl, and

36) heterocyclysulfonylaminocarbonyl,

wherein Ar is a substituted aryl or substituted heteroaryl group, where  
substitutions are independently selected from

a. hydrogen,

b. halogen,

c. alkyl,

d. aryl,

e. haloalkyl,

f. hydroxy,

g. alkoxy,

h. alkoxyalkyl,

i. alkoxycarbonyl,

j. alkoxyalkoxy,

k. hydroxyalkyl,

l. aminoalkyl,

m. aminocarbonyl,

n. alkyl(alkoxycarbonylalkyl)aminoalkyl,

o. heterocyclyl,

p. substituted heterocyclyl,

q. heterocyclylalkyl,

r. substituted heterocyclylalkyl,

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- s. carboxaldehyde,
- t. carboxaldehyde hydrazone,
- u. carboxamide,
- v. alkoxycarbonylalkyl,
- w. carboxy,
- x. carboxyalkyl,
- y. carboxyalkoxy,
- z. carboxythioalkoxy,
- aa. carboxycycloalkoxy,
- bb. thioalkyl,
- cc. hydroxycarbonylalkyl (carboxyalkyl),
- dd. hydroxyalkylaminocarbonyl,
- ee. cyano,
- ff. amino,
- gg. heterocyclylalkylamino,
- hh. carboxyalkylamino,
- ii. heterocyclylalkylaminocarbonyl, and
- ii. "trans-cinnamide," and

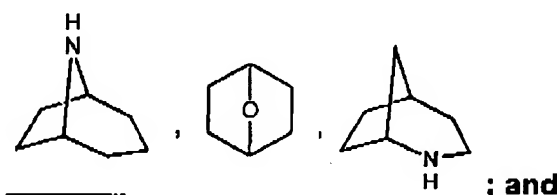
wherein the heterocyclyl is chosen from 4-, 5-, 6- and 7-membered rings containing 1-3 heteroatoms independently selected from nitrogen, oxygen and sulfur; the 4- and 5-membered rings have zero to two double bonds and the 6- and 7-membered rings have zero to three double bonds, the heterocyclyl being optionally substituted with alkyl, halogen, hydroxy or alkoxy substituents,



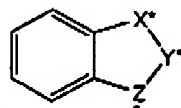
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wherein the heterocyclyl optionally comprises a group chosen from:

- (i) bicyclic, tricyclic and tetracyclic groups in which any of the above heterocyclic rings is fused to one or two rings independently selected from an aryl ring, a cyclohexane ring, a cyclohexene ring, a cyclopentane ring, a cyclopentene ring, and another monocyclic heterocyclic ring;
- (ii) bridged bicyclic groups where a monocyclic heterocyclic group is optionally bridged by an alkylene group selected from



; and



- (iii) compounds of the formula

where X\* and Z\* are

independently selected from -CH<sub>2</sub>-, -CH<sub>2</sub>NH-, -CH<sub>2</sub>O-, -NH- and -O-, with the proviso that at least one of X\* and Z\* is not -CH<sub>2</sub>-, and Y\* is selected from -C(O)- and -(C(R''))<sub>v</sub>-, where R'' is hydrogen or alkyl of one to four carbons, and v is 1-3;

wherein aryl is defined as a mono- or bicyclic carbocyclic, aromatic ring,

and wherein the compound is administered orally, rectally, parenterally,

intracisternally, intravaginally, intraperitoneally, topically, buccally, or as an oral or nasal spray.

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33. (currently amended) A method of treating cerebral vasospasm according to Claim 32 comprising the administration of a composition of Claim 19 to a mammal in need of treatment, wherein the compound is administered as a part of a composition, wherein the composition further comprises a pharmaceutically acceptable carrier or excipient.